REMARKS

Claims 1-3, 6-22 and 24-37 are pending in the application. Claims 20, 21, 25, 28, 29, 35 and 36 are withdrawn pending rejoinder. Applicants herewith amend claim 1, support for which is found, *inter alia*, at paragraph 2 of the specification. Applicants herewith amend claims 8 and 16, support for which is found, *inter alia*, at original claim 1. No new matter is added. Entry of the Amendment is kindly requested.

I. Priority

Applicants thank the Examiner for acknowledging priority to U.S. Application No. 10/170,390. At page 3 of the Office Action, the Examiner asserts that claims 1-3, 6-19, 22, 24-27, 30-34 and 37 are not accorded the benefit of priority because the claims allegedly lack a written description and lack enablement and because claims 2, 17, 30 and 32-34 are not described by the specification.

Applicants disagree. The specification of the present application discloses the claimed agents by virtue of their incorporation by reference thus, the specification complies with 35 U.S.C. §112, the M.P.E.P. § 2163.07 and *Ex parte Maziere* (Appeal No. 92-3407), as further discussed in detail in Section VII herein. The issues of enablement and written description are also specifically addressed in significant detail below, at least at Sections VI-VIII and IV-X. Accordingly, Applicants request that the Office acknowledge Applicants' priority for claims 1-3, 6-19, 22, 24-27, 30-34 and 37.

II. The 37 C.F.R. § 1.132 Declarations Are Proper

At page 4 of the Office Action, the Office alleges that the Declarations submitted under 37 C.F.R. § 1.132, filed April 16, 2007 and August 24, 2007 are not duly executed and therefore

cannot be considered. More specifically, the Examiner asserts that the Declaration by Dr. Rajeeva Singh, filed August 24, 2007, is improper for lack of execution.

Applicants thank the Examiner for considering the unexecuted Declaration. The executed Declaration of Dr. Singh was filed September 28, 2007. Dr. Singh's Declaration is identical in substance to the Declaration executed by Nancy Dagdigian, filed August 24, 2007. Thus, the Declarations are proper under 37 C.F.R. § 1.132. Collectively, the Declarations are sufficient to overcome the § 102(a) rejection based on Maloney *et al.*[1] Withdrawal of the objection to the Declarations and withdrawal of the § 102(a) rejection is therefore respectfully requested.

IV. The Specification is Proper Under MPEP §608.01(v)

At page 4 of the Office Action, the Examiner maintains the objection to the specification, because of absent trademark indicators. Applicants herewith amend the specification to include trademark indicators. The Amendment overcomes the objection. Withdrawal of the objection is therefore respectfully requested.

V. The Request for Rejoinder of Claims 22, 30, 31 and 34 is Maintained

At page 5 of the Office Action, the Office objects to claims 22, 30, 31 and 34, as being drawn to a non-elected invention (i.e., the claims corresponding to Group III). Applicants maintain their request for rejoinder, as a matter of right, of the claims of Group III, upon allowance of the elected product claims pursuant to M.P.E.P. § 821.04.

[1] At page 2 (Continuation Sheet) of the Interview Summary issued September 18, 2007, the Examiner admits that presentation of the executed Declaration of Dr. Singh would moot the § 102(a) rejection.

VI. Claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 are Adequately Described Under 35 U.S.C. § 112, First Paragraph

At page 5 of the Office Action, the Office rejects claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 under 35 U.S.C. § 112, first paragraph, for allegedly lacking a written description. The Examiner alleges that the ordinary skilled artisan does not appreciate that the Applicants had possession of the claimed invention because the specification lacks sufficient structural features of the claimed antibodies and because there is no additional disclosure of antibody variants.

Applicants respectfully disagree. As indicated in the prior Response dated April 16, 2007, the specification includes specific examples of sequence homologues (i.e., claim 15 recites four homologues of the light chain; claim 16 recites one heavy chain homologue; and the specification provides adequate written description of the homologues, *inter alia,* at paragraph 67). In addition, EM164 was sequenced and humanized and was determined to have heavy chain variable region sequences which are set forth in SEQ ID NOS.:7 (murine) and 9 (humanized), and light chain variable region sequences which are set forth in SEQ ID NOS:8 (murine) and 10 (humanized). The specification also teaches antibodies or fragments thereof produced by, at least, mutation, deletion and/or insertion within the variable and/or constant region sequences that flank a particular set of CDRs (paragraph 68) or polypeptides (e.g., antibodies) with amino acids substantially the same as the amino acid sequence of the variable or hypervariable regions of the antibodies of the invention (paragraph 71). Furthermore, the specification teaches that "[t]he variability is not usually evenly distributed through the variable domains of the antibodies. It is typically concentrated in three segments called complementarity determining regions (CDRs) or hypervariable regions both in the light chain and the heavy chain variable domains." See paragraph 68, column 6, lines 4-9. The CDR sequences are taught at least by SEQ ID

NOS:1-6 and are encompassed in the heavy chain and the light chain variable region sequences set forth. The specification teaches mutation, deletion and/or insertion within the variable and/or constant region sequences that flank a particular set of CDRs (paragraph 63) and teaches an assay for determining binding activity of the antibody to the IGF-IR (for example, see paragraph 117 under the title "Binding Characterization of EM164 Antibody").

Furthermore, the claims encompass antibodies with the same specificity as EM164, wherein the antibodies have in the heavy chain variable region at least 90% sequence identity to an amino acid sequence set forth in SEQ ID NOS:7 or 9 or in the said light chain variable region at least 90% sequence identity to an amino acid sequence set forth in SEQ ID NOS:8 or 10 and specifically bind to IGF-IR.

The invention has at least two additional aspects, the first being an antibody that comprises a heavy chain variable region defined by at least SEQ ID NOS:7 or 9 or that comprises a light chain variable region defined by at least SEQ ID NOS:8 or 10 and the second being an antibody in which the heavy chain variable regions retain the specificity of at least SEQ ID NOS:7 or 9 or in which the light chain variable regions retain the specificity of at least SEQ ID NOS:8 or 10. The specification teaches an antibody having a heavy chain variable region defined by at least SEQ ID NOS:7 or 9 or a light chain variable region defined by at least SEQ ID NOS:8 or 10 or additional EM164 specific antibodies or fragments thereof having 90% identity to the heavy chain variable region defined by at least SEQ ID NOS:7 or 9 or a light chain variable region defined by at least SEQ ID NOS:8 or 10 and having binding affinity to IGF-IR. The procedures for making such antibodies or fragments containing the heavy chain variable region defined by SEQ ID NOS:7 or 9 or a light chain variable region defined by at least SEQ ID NOS:8 or 10 are taught and known in the art as illustrated by the specification. An assay

is taught that identifies other antibodies having the claimed IGF-IR binding specificity. Moreover procedures for making antibodies or fragments containing the heavy chain variable region defined at least by SEQ ID NOS:7 or 9 or a light chain variable region defined at least by SEQ ID NOS:8 or 10 that have 90% identity to the heavy chain variable region defined at least by SEQ ID NOS:7 or 9 or a light chain variable region defined at least by SEQ ID NOS:8 or 10, which retain specificity, are known in the art. The specification explicitly states that all varieties must confer binding activity and must have at least 90% identity to the variable regions (paragraph 71). Thus, there is sufficient description of the claimed genus of antibodies to reasonably convey to one of ordinary skill the art that the inventors possessed the claimed invention. The Office is respectfully reminded that to meet the goal of reaching a clearly defined issue for an early termination of proceedings, i.e., issuance of an Office Action or Allowance of claims, the Examiner is charged with conducting a careful and thorough search and fully applying the references in preparing the first Office Action on the merits in order for a speedy and just determination of the issues involved in the examination of the application. *See* MPEP §§ 706.07 and 904.03 and page 4, first full paragraph, Synopsis of Application of Written Description Guidelines. The specification and claims were not duly considered prior to issuance of the outstanding Office Action because the character of IGF-IR and the scope of the claims (i.e., IGF-IR binding antibodies) was not duly considered. Applicants therefore kindly request that the rejection be withdrawn as premature.

The policy of the Office is that the level of skill and knowledge in the art of making antibodies is such that the production of antibodies to well-characterized antigens is mature. Example 16, page 59, Synopsis of Application of Written Description Guidelines. The Office does not allege that IGF-IR is not well-characterized. Applicants establish the opposite.

Background of the Invention, paragraphs 3 to 17, Specification. The polypeptide to which the claimed antibodies bind is specifically set forth at least at paragraphs 120-126 of the specification and the antigen is further defined by the Applicants by virtue of the antibody interactions directed thereto (i.e., as disclosed, *inter alia*, at pages 55-69 of the specification). The claims are directed to antibodies that bind IGF-IR and do not include within their scope antibodies that do not bind to IGF-IR.[2] Because the Office's policy indicates that claims directed to antibodies that bind well characterized antigens meet the requirements of 35 U.S.C. §112, first paragraph the rejection is improper and should be withdrawn.

At page 9 of the Office Action, the Examiner relies on *Reagents of the University of Californina v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997) as support for his position that substantial structural features common to all claimed antibodies must be disclosed in the specification. However, the Examiner improperly states Applicants' burden under current law. In *Falkner v. Inglis* (79 USPQ2d 1001) the Court declared, "specifically, we hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure" and ". . . it is the binding precedent of this Court that *Eli Lilly* does not set forth a *per se* rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art." Emphasis in original.

[2] At page 8 of the Office Action, the Examiner incorrectly asserts that a functional feature shared by the claimed genus is absent from the specification however, the claims explicitly recite binding to IGF-IR.

Because the Examiner fails to give due consideration to Applicants' disclosure and fails to apply the appropriate legal standard for examining the outstanding claims, withdrawal of the lack of written description rejection is respectfully requested.

VII. Claims 2, 17, 30 and 32-34 Do Not Introduce New Matter Under 35 U.S.C. § 112, First Paragraph

At page 10 of the Office Action, the Office rejects claims 2, 17, 30, and 32-34 under 35 U.S.C. § 112, first paragraph, for allegedly introducing new matter into the specification (i.e., specifically, thalidomide, carmustine, pamidronate, prednisone, erythropoietin and bisphosphonate) because the specification allegedly fails to particularly point to the disclosure of these compounds in the reference that was incorporated by reference into the specification.

Applicants respectfully disagree. In the Office Action issued June 15, 2007, the Examiner asserted that "[the] introduction of less than the entirety of the above reference [DeVita et al.] into the specification would be considered new matter," a position that implies that introduction of the entire reference would not raise a new matter rejection.

It is contradictory to maintain that the introduction of portions of a reference that the Office admits can be properly introduced in its entirety somehow introduce new matter into the specification however, this appears to be the Office's position. The Office's position is also contrary to settled law. Rule 37 C.F.R. § 1.57 states that incorporation by reference is accomplished by expressing a clear intent to incorporate by reference (i.e., by using the words "incorporate" and "reference") and by clearly identifying the referenced information (i.e., a patent, application or publication). The M.P.E.P. clearly states, "an application may attempt to incorporate the content of another document or *part thereof* by reference to the document in the text of the specification. The information incorporated is as much a part of the application as

filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed." Emphasis added. M.P.E.P. § 2163.07(b).

Applicants express a clear intent to incorporate by reference the content of the publications cited in the specification. Page 69, Specification. At paragraph 93 of the specification, Applicants explicitly identify the incorporated publication DeVita et al. Thus, the April 16, 2007 Amendment to the specification incorporating DeVita et al. is in compliance with 37 C.F.R. § 1.57.

Furthermore, in *Ex parte Maziere* (Appeal No. 92-3407), the Board held that "[t]he Applicants of [the Maziere application] were quite correct in not further burdening the record of that file by including the text which was incorporated by reference." The present facts resemble those at issue in *Ex parte Maziere* wherein the Office objected to Applicant's incorporation by reference of essential material into a continuation application via a "compressed statement" of incorporation. Page 2-3, *Ex parte Maziere*. The subject matter claimed in the continuation application at issue (for which incorporation was necessary) was not claimed in the parent application however, the Board concluded that the subject matter was properly introduced into the continuation application in which the subject matter was claimed because, "to the extent that present practice would not allow incorporation by reference of 'essential matter' in a pending patent application, the Br* subject matter was not such essential material in parent Serial No. 07/072,090 since it was not claimed therein. The Applicants...were quite correct in not further burdening the record of that file by including the text which was incorporated by reference." Page 3, *Ex parte Maziere*.

Consistent with 35 U.S.C. §112, first paragraph, M.P.E.P. § 2163.07 and the holding of the Board in *Ex parte Maziere*, Applicants' incorporation by reference is proper. Therefore, withdrawal of the new matter rejection is kindly requested.

VIII. Claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 are Enabled Under 35 U.S.C. § 112, First Paragraph

At pages 12 and 13 of the Office Action, the Office rejects claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 under 35 U.S.C. § 112, first paragraph, for lacking enablement because the Statement of Availability is allegedly defective, the claims include within their scope antibodies comprising fewer than six CDRs whereas the disclosure allegedly does not include examples of antibodies with fewer than six CDRs, and the claims include within their scope antibody variants whereas the disclosure allegedly does not include examples of antibody variants.

Applicants disagree. Regarding the first aspect of the rejection, Applicants herewith attach a Statement of Availability fully compliant with 37 C.F.R. § 1.808. The Statement of Availability overcomes the rejection. Withdrawal of the lack of enablement rejection is therefore respectfully requested.

Regarding the second aspect of the rejection, the Examiner admits that the specification is enabling for a composition comprising an antibody or antibody fragment that specifically binds to IGF-I-R, wherein the antibody comprises the six CDRs of SEQ ID NO:1 to NO:6. Page 13, Office Action. The Examiner asserts that the claims are not enabled for antibodies that bind to IGF-IR (i.e., the same specificity as EM164) with fewer than six CDRs or contain any variation among their sequences. To buttress his argument the Examiner improperly relies on antiquated references that were published more than a decade prior to Applicants' filing date and demonstrate the opposite of that which he concludes. For example, the Examiner cites Rudikoff

et al. and Watkins *et al.* to prove that it is highly unpredictable which antigen an antibody will bind based on homology alone however, the Rudikoff *et al.* states the opposite. Rudikoff *et al.* disclose that SI07 subclones are vastly antigen reactive, since only "0.1-1%" of the clones do not precipitate in soft agar assays. Page 1980, Results and Discussion, first sentence. Furthermore, at page 1982, the researchers conclude, "[w]e have characterized another primary variant of S107 that has decreased antigen binding and a single amino acid substitution in the fifth residue of its J segment (39). However, it is clear that all substitutions need not and probably do not affect antigen binding. For example, the heavy chain from the P-Cho-binding myeloma protein M167 (35) differs from that of S107 at 13 positions (8 in hypervariable regions including a size difference) and yet has an association constant for hapten only slightly lower than S107. We have previously shown that, among anti-1,6-galactan-binding myeloma proteins, as many as eight or nine substitutions may occur in hypervariable regions with no significant effect on hapten affinity or specificity." Emphasis added. Thus, the reference as cited by the Examiner is an anomaly, and not representative of the state of the art, nor the Examiner's position.

Regarding Watkins et al., even if the antibodies of Watkins *et al.* bind collagen, at no point do Watkins *et al.* suggest or demonstrate that the antibodies do not bind IGF-IR. Cross-reactive antibodies are known in the art.

To buttress his position, the Examiner asserts that "the art cited by Applicants is directed to domain antibodies from camelids, which have evolved to exist as single domain antibodies, whereas the instant specification discloses antibodies that naturally comprise a VH-VL pair." However, single chain antibodies from camelids are merely a single perspective of the state of

the art. Functional variants and antibodies with fewer than six CDRs are known in the art.[3] For example, on page 527, Aires da Silva *et al.* disclose the production of rabbit anti-Vif VH single-domain antibodies. Further, Tanaka *et al.* disclose the use of intracellular antibody capture using scFc phage antibody libraries, to isolate single-domain VH "intrabodies," which have been demonstrated to possess greater affinity for antigen than the parental antibody containing heavy and light chains. Page 1110, column 2, lines 44-48. Further, Tanaka *et al.* conclude that "binding of the anti-RAS scFv33 to antigen can occur through the VH domain alone." Page 1110, column 2, last sentence. Further still, on page 1115, column 2, first full paragraph, Tanaka *et al.* disclose that isolated VH domains are "ideal for binding specifically and with high affinity to antigen *in vivo*" and that "VL alone should possess the same property." Peterson *et al.* disclose that "a CDR is the smallest functional unit of an antibody" and states, "[T]he smallest functional unit of an antibody to be produced has been the CDR peptides . . . which can vary from eight to 20 amino acids" (page 314-315 and Figure 1C). Peterson further states that "[t]he affinity of a CDR is tested by its ability to compete with the parental antibody at its binding site. Berezov and colleagues (2001) demonstrated that a peptide designed from the sequence of the third CDR of an anti-Her2/neu antibody heavy chain sequence was able to bind to the receptor and disable its tyrosine kinase activity. Another biologically active peptide derived from an antineurokinin receptor antibody by Wijkhuisen and coworkers (2003) was capable of antagonizing substance P-induced cAMP production." Peterson at page 315. See, Advances in Monoclonal Antibody Technology: Genetic Engineering of Mice, Cells and Immunoglobulins,

[3] A patent disclosure need not enable information within the knowledge of an ordinarily skilled artisan. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, (Fed. Cir. 2004), petition for cer. Filed, Oct. 4, 2004. Extensive screening to isolate a claimed cell was not undue when the required methods are routine in biotechnology. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

Peterson NC, ILAR J. 46(3):314-319 (2005). Park et al., discloses AHNP which "is comparable in potency to the full-length monoclonal antibody and exhibits biochemical and biological properties that are predictive of therapeutic use." Page 194, second column, sentences 1-7. The reference further states, "the general approach described here may be considered a paradigm for development of specific receptor-based therapies..." The *general approach* is referenced to date back to as early as 1996 (see reference 19, Zhang et al.). Please note that AHNP was extensively analyzed and found to inhibit cell proliferation and anchorage independent growth (Figure 2); enhance apoptosis (Figure 4); and inhibit in vivo tumor growth (Figure 5). U.S. Patent No. 6,926,893, states, "another form of an antibody fragment is a peptide coding for a single [CDR] can be obtained by constructing genes encoding the CDR of an antibody of interest." Col. 9, lines 43-47.

The Examiner's position is also contradictory to the Board's precedential decision, *Ex parte Kubin* (Appeal No. 2007-0819), wherein the Examiner rejected claims containing "at least 80% identity to" language in the absence of working examples by relying upon scientific literature that allegedly suggested that very small changes in a sequence, even one amino acid, result in a different function. In *Ex parte Kubin* claims directed to "polypeptides at least 80% identical to amino acids 22-221 of SEQ ID NO:2" were found enabled by the Board. The Board withdrew the Examiner's rejection because the amount of experimentation required to practice the claimed invention might have been extensive but would have been routine. The Board acknowledged that the specification did not disclose any variant of SEQ ID NO:2 within amino acids 22-221 however, the Board acknowledged the high skill level in the field, that the methods for making and screening the variant sequences were known in the art, and concluded that "the

experimentation involved to produce other sequences within the scope of the claims would have been well within the skill of those in the art," and thus routine.

Thus, contrary to the Examiner's position, the references establish that prior to Applicants' filing date the state of the art of antibody production was such that a person of ordinary skill in the art would conclude, without question, that an antibody could be routinely made and used from a single CDR and that variations of an antibody wherein functional antibodies are obtained is routine in the art.

Withdrawal of the enablement rejection is therefore respectfully requested.

IX. Claims 1, 6, 19, 22, 24 and 26 are Novel Over Zia *et al.*

At page 17 of the Office Action, the Office rejects claims 1, 6, 19, 22, 24 and 26 under 35 U.S.C. 102(b) as allegedly being anticipated by Zia *et al.* (*Journal of Cellular Biochemistry,* Supplement 24:269-275, 1996).

Applicants respectfully disagree. Amended claim 1 recites antibodies which bind IGF-IR, which have the same binding specificity as the EM164 antibody, and which are substantially devoid of agonist activity. The antibody disclosed by Zia *et al.* is an alpha IR-3 antibody with significant agonist activity, as evidenced by Kato *et al.*, who describe the same alpha IR-3 antibody as Zia *et al.* as inducing receptor autophosphorylation, activating phosphatidylinositol-3-kinase and 2-deoxyglucose uptake, inducing ornithine decarboxylase gene expression, and stimulating thymidine incorporation. (See Kato *et al.*, throughout). These results are further confirmed by an independent laboratory using the same alpha IR-3, in which antibody alpha IR-3 was capable of mimicking the ability of IGFI to stimulate three different biological responses in the CHOIGFIR cells. (See Steele-Perkins *et al.*, page 11491). In fact, the investigators concluded that alpha IR-3 stimulated the serine phosphorylation of the receptor

(Fig. 5). "This is further evidence that the antibody is capable of stimulating the same responses as IGF-I." Consistent with these prior studies, Zia *et al.* point out that the alpha IR-3 antibody was not potent in inhibiting breast tumors.

Accordingly, as the antibody of Zia *et al.* possesses substantial agonist activity and does not have the same specificity as Applicants' EM164 therefore, the reference as cited by the Examiner fails to anticipate Applicants claimed invention. Accordingly, withdrawal of this rejection is kindly requested.

X. Claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 are Novel Over Maloney *et al.*

At page 18 of the Office Action, the Office rejects claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 under 35 U.S.C. 102(a) as anticipated by Maloney *et al.*

The executed Declarations filed September 28, 2007, and August 24, 2007, overcome the rejection. Page 4, Office Action. Withdrawal of the rejections is therefore respectfully requested.

XI. Claims 1, 6, 19, 22, 24 and 26 are Novel Over Rohlik *et al.*

At page 18 of the Office Action, the Office rejects claims 1, 6, 19, 22, 24 and 26 under 35 U.S.C. 102(b) as anticipated by Rohlik *et al.* (*Biochemical and Biophysical Research Communications* 149:276-281, 1987).

Applicants respectfully disagree. Rohlik *et al.* disclose an alpha IR-3 antibody (see the detailed discussion of the alpha IR-3 antibody in Section IX, herein). The alpha IR-3 antibody exhibits substantial agonist activity. Since the alpha IR-3 antibody does not have the same specificity as Applicants' EM164 the antibody of Rohlik *et al.* cannot anticipate Applicants' claimed invention. Accordingly, withdrawal of the rejection is respectfully requested.

XII. Claims 1-2 and 32 are Novel Over Rohlik *et al.* in view of Teicher *et al.*

At page 20 of the Office Action, the Office rejects claims 1-2 and 32 under 35 U.S.C. 103(a), as allegedly being unpatentable over Rohlik *et al.* in view of Teicher *et al.* (*Clinical Cancer Research* 5:2638-2645, 1987).

Applicants respectfully disagree. As discussed above (i.e., in section XI) the alpha IR-3 antibody disclosed by Rohlik *et al.* exhibits substantial agonist activity and does not have the same specificity as Applicants' EM164 antibody. Rohlik *et al.* does not disclose Applicants' claimed antibody. Teicher *et al.* does not compensate for the deficiencies of Rohlik *et al.* since Teicher *et al.* as cited by the Examiner only discloses the use of bortezomib as a proteasome inhibitor. Teicher *et al.* does not disclose an anti-IGF-R antibody substantially devoid of agonist activity therefore a *prima facie* case of obviousness cannot possibly be established. Withdrawal of the obviousness rejection is therefore respectfully requested.

XIII. The Provisional Rejections of Claims 1-3, 6-18, 19, 22, 24, 26, 27 30-34 and 37 are Held in Abeyance

At page 21 of the Office Action, the Office provisionally rejects claims 1-3, 6-18, 32-33 37, and specifically claims 19, 22, 24, 26, 27, 30, 31 and 34 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of copending Application No. 10/170,390 and Teicher *et al.* Applicants elect to hold the provisional rejection in abeyance.

IVX. The Amendment Filed April 16, 2007 Is Proper Under 35 U.S.C. § 132(a)

At page 22 of the Office Action, the Office objects to the Amendment filed April 16, 2007 under 35 U.S.C. 132(a) for allegedly introducing new matter into the disclosure.

Applicants respectfully disagree. Applicants incorporate the argument set forth in Section VI, herein and assert that the Amendment filed April 16, 2007 is proper under 35 U.S.C. §112, first paragraph, M.P.E.P. § 2163.07, 35 U.S.C. 132(a) and Board precedent. Withdrawal of the new matter rejection is kindly requested.

XV. Claims 1 and 37 are Novel Over Zia *et al.* in view of Queen *et al.*

At page 25 of the Office Action, the Examiner rejects claims 1 and 37 under 35 U.S.C. 103(a) as being unpatentable over Zia *et al.* in view of Queen *et al.*

Applicants respectfully disagree. As noted above in section IX, the alpha IR-3 antibody disclosed by Zia *et al.* has substantial agonist activity and does not have the same specificity as Applicants' EM164. Zia *et al.* as cited by the Examiner do not disclose Applicants' claimed antibody. Queen *et al.* fail to compensate for the deficiencies of Zia *et al.* since Queen *et al.* as cited by the Examiner fails to disclose an anti-IGF-R antibody that is substantially devoid of agonist activity. Thus, a *prima facie* case of obviousness cannot possibly be established based on the reference as cited by the Examiner. Withdrawal of the objection is therefore respectfully requested.

XVI. Claims 1 and 37 are Novel Over Rohlik *et al.* in view of Queen *et al.*

At page 25 of the Office Action, the Office rejects claims 1 and 37 under 35 U.S.C. 103(a) as being unpatentable over Rohlik *et al.*, in view of Queen *et al.* The Examiner asserts that Rohlik *et al.* disclose the murine monoclonal antibody alpha IR-3 which specifically binds to the insulin-like growth factor I receptor. The Examiner admits that Rohlik *et al.* do not disclose humanization of the alpha IR-3 antibody, but alleges that this deficiency is made up for in the teachings of Queen *et al.* The Examiner concludes that it would have been *prima facie* obvious

to one of ordinary skill in the art at the time the claimed invention was made to humanize the IR-3 antibody of Rohlik *et al.* in view of Queen *et al.* to arrive at Applicants' claimed invention.

Applicants respectfully disagree. As noted above is section XI, the alpha IR-3 antibody disclosed by Rohlik *et al.* has substantial agonist activity and does not have the same specificity as Applicants' EM164. Thus, Rohlik *et al.* do not disclose Applicants' claimed antibody. Queen *et al.* fail to remedy the deficiencies of Rohlik *et al.* since Queen *et al.* as cited by the Examiner disclose methods of humanization. Queen *et al.* fail to disclose an anti-IGF-R antibody that is substantially devoid of agonist activity. Thus, a *prima facie* case of obviousness cannot possibly be established based on the reference as cited by the Examiner. Withdrawal of the obviousness rejection is therefore respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

William J. Simmons, Ph.D.
Registration No. 59,887

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860
WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: March 18, 2008